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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/536,736	03/28/2000	Helge Bastian	C12Q1/68	5490

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EXAMINER	
GUZO, DAVID	

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1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/536,736	BASTIAN ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-17,22,24-31,33-40,51,53-57,59-66,69-74 and 76-91* is/are pending in the application.

4a) Of the above claim(s) *6-8,56 and 57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,9-17,22,24-31,33-40,51,53-55,59-64,69-74 and 76-91* is/are rejected.

7)☒ Claim(s) *65-66* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 5/18/07 has been entered.

Claims 6-8 and 56-57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/17/02.

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-5, 24, 25, 33, 34, 36, 51, 69, 72, 76-80, 82, 90 and 91 are rejected under 35 U.S.C. 102(b) as being anticipated by Ogawa et al.

Applicants claim a process for isolating nucleic acids comprising charging a non-siliceous membrane from a given direction with nucleic acids wherein the membrane has two opposing sides, immobilizing the nucleic acids on one side of the membrane by binding the nucleic acids to the membrane in the presence of an immobilization buffer, releasing the immobilized nucleic acids from the membrane by applying an elution agent wherein the nucleic acids do not pass through to the other side of the membrane, removing the released nucleic acids from the same side of the membrane on which the nucleic acids were bound wherein the released nucleic acids are removed without retrieving materials which have contacted the other sided of the membrane surface.

Ogawa et al. (previously cited and of record, see whole document, particularly columns 2-4, claims 1-5) recites a process for isolating nucleic acids comprising charging (loading) a non-siliceous membrane (which can be a hydrophobic material such as polysulfone, pore sizes can be from 0.005 to 0.45 microns in diameter) which possesses two opposing sides, immobilizing the nucleic acids on one side of the membrane in the presence of an immobilization buffer (which can contain ethanol or methanol), washing the membrane with a buffer such as TE (which contains water) wherein the buffer is drawn through the membrane by suction (pressure), releasing the nucleic acids from the membrane by use of an elution buffer (TE) wherein the nucleic acids do not pass through to the other side of the membrane (elution buffer applied to one side of the membrane, shaken and recovered by use of a pipette) wherein the nucleic acids are removed without retrieving materials which have contacted the other side of the membrane. Ogawa et al. therefore teaches the claimed invention.

35 USC 103(a) Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-14, 39, 40, 55, 59-61, 70-72, 77-78 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogawa et al. in view of Mullis (US 5,234,824).

Applicants' invention is as described above. Additionally, applicants recite that the immobilization buffer includes aqueous solutions of alkaline and alkaline earth metals with mineral acids or hydroxyl derivatives of aliphatic or acyclic saturated or unsaturated hydrocarbons, the membrane can be either hydrophobic or hydrophilic (i.e. cellulose acetate or polyvinylidene, polycarbonate, etc.), the process for purifying the nucleic acids is carried out on a multi-well plate, the washing step uses solutions of alkaline and alkaline earth metals with mineral acids or a chaotropic agent, the unbound

fluid components of the mixture or wash are drawn through the membrane, the membrane can have pores in the range of 0.001 to 50 micrometers or 0.01 to 20 or 0.05 to 10 micrometers in diameter, that at least one chemical reaction is carried out on the nucleic acids between the release and removal steps, etc.

Ogawa et al. teaches the essential features of the claimed invention. Ogawa et al. teaches that standard methods of removing proteins and other materials from nucleic acids can be used in the immobilization solutions prior to the nucleic acids being applied to the filters and that solutions to be used in washing the filters are not restricted. However, Ogawa et al, does not explicitly teach the standard components of the immobilization and washing solutions which are routinely used to prepare nucleic acid containing compositions for immobilization on membranes and wash the filters containing the immobilized nucleic acids or the use of hydrophilic membranes or the chemical treatments of nucleic acids between the time the nucleic acids are released from the membrane and the time they are collected.

Mullis et al. (previously made of record, see whole document, particularly the Abstract; last paragraph in column 2; columns 5-6; examples 6-8 and Claims 1-12) teaches some of the standard immobilization and washing solutions used in processes for isolating nucleic acids comprising charging (loading) a non-siliceous membrane (which can be a hydrophobic or hydrophilic membrane) which can contain pore sizes can be from 0.2 to 0.8 microns in diameter, which possesses two opposing sides, immobilizing the nucleic acids on one side of the membrane in the presence of an immobilization buffer (which can contain polyvinyl alcohol, sodium chloride, disodium

hydrogen phosphate, potassium dihydrogen phosphate, magnesium chloride, potassium chloride, etc. within the pH 3-11 range), washing the membrane with water or a buffer such as those recited in Table 3 or in Example 7 (wherein the elution solutions can contain a chaotropic agent such as ammonium sulfate as well as Tris-HCl, magnesium chloride, $ZnCl_2$, $(NH_4)_2$ (SO_4), etc.).

It would have been obvious for the skilled artisan, seeking to choose immobilization and wash solutions for use in the methods for purifying nucleic acids recited by Ogawa et al., to choose the immobilization and washing solutions taught by Mullis because said solutions are standard in methods for purifying nucleic acids, wherein said methods involve binding the nucleic acids to membranes which can be hydrophobic or hydrophilic. Furthermore, Mullis teaches that the nucleic acids can be subject to restriction endonuclease digestion after release from the membranes to determine the levels of release and recovery of the nucleic acids from the filters. The ordinary skilled artisan would have been motivated to combine the teachings of Ogawa et al. on the purification of phage nucleic acids with the teachings of Mullis on the use of standard nucleic acid immobilization and washing solutions for use with hydrophobic or hydrophilic membranes because Mullis teaches that said solutions can be routinely used in processes for purifying nucleic acids on membranes. The ordinary skilled artisan would have been motivated to digest the nucleic acids released from the filters in order to measure the level (and purity) of recovery of the nucleic acids using various modifications of the immobilization and washing techniques. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant

invention was made, it must be assumed that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 9-17, 22, 26-31, 35, 37-40, 53-55, 59-64, 70, 71, 73-74, 81 and 83-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogawa et al. in view of Mullis et al., Pfister et al., Boom et al., Colpan et al. and Marfarlane et al.

Applicant's invention is as described above. In addition, applicants claim that the immobilization buffer contains a phenol or polyphenol or chaotropic agents such as guanidinium isothiocyanate at 0.01 to 5 or 7-molar levels and various hydrophobic membranes or surfaces coated with hydrophobic substances for use in the claimed process for isolating nucleic acids, and wherein the washing solution contains an alcohol or phenol, etc.

Ogawa et al. Mullis et al. are applied as above. Pfister et al. and Boom et al. have been applied as in the previous Office Action (mailed 8/23/06). Ogawa et al., Mullis et al., Pfister et al. and Boom et al. do not explicitly teach the concentrations of chaotropic agents used in the immobilization buffers or the use of malonic, oxalic, succinic or citric acid or phenol in said buffers or use of alcohols in the washing buffer.

Colpan et al. (US 6,383,393, issued 5/7/02, filed 3/15/96, see whole document, particularly columns 2-5) teaches the use of chaotropic agents (such as guanidinium isothiocyanate, potassium iodide, sodium perchlorate, etc.) at levels of 1-8-molar in the immobilization buffer as well as use of alcohols and phenol in the immobilization buffer.

Macfarlane (US 5,985,572, issued 11/16/99, filed 2/23/98, priority to 8/27/93, see whole document, particularly columns 2-4, Example 3, etc.) teaches use of salts of oxalic, malonic citric or succinic acid (i.e. sodium citrate) in nucleic acid purification protocols.

The essential features of applicants' invention are taught by Ogawa et al. (see above 102(b) rejection). The remaining limitations relate to the standard procedures and components used in nucleic acid purification techniques (i.e. the types of membranes used, the standard solutions (immobilization buffers) used to solubilize compositions comprising the nucleic acids of interest as well as the agents used in said solutions and in washing buffers to wash the membranes after the nucleic acids are applied. All of the components of the immobilization solutions claimed by applicants, such as chaotropic agents including guanidinium isothiocyanate, potassium perchlorate, etc., as well as agents such as alcohols, phenol, salts of organic dicarboxylic acids (i.e. citric acid, oxalic acid, etc.) and the agents used in washing solutions (i.e. containing an alcohol, phenol, etc.) are standard components in procedures for isolating nucleic acids (as evidenced, for example, by the teachings of Colpan et al. and Macfarlane. The prior art likewise teaches that any suitable membrane (usually hydrophobic but can be hydrophilic) can be used to bind nucleic acids and the membranes claimed by applicants are all either hydrophobic or hydrophilic. Since the prior art teaches that many nucleic acids preferentially bind to hydrophobic surfaces (hence the use of hydrophobic membranes such as polysulfone or polycarbonate, etc. in the cited prior art), the use of membranes which are hydrophobic or are coated with hydrophobic

substances must be considered obvious to the ordinary skilled artisan. The choice of the prior art membranes or membranes having hydrophobic surfaces, absent evidence to the contrary, appears to be merely a matter of optimization or design choice which constitutes routine experimentation. Indeed, given the highly developed nature of the prior art in the area of nucleic acid purification and the well known solutions used in extracting and purifying nucleic acids as well as the membranes or filters used to bind or retain the nucleic acids (as evidenced by the cited prior art), the ordinary skilled artisan would have been motivated to employ any of the instantly claimed limitations concerning immobilization and washing solutions and nucleic acid binding membranes or filters as any of said solutions and membranes or filters would serve to purify nucleic acids and said compositions and procedures are used for their known and expected results. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be assumed that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Applicants' arguments and the Declaration pursuant to 37 CFR 1/132 of Owe Oelmuller, filed 5/18/07, are rendered moot by the withdrawal of the previous ground of rejection and the application of new grounds of rejection under 35 USC 102(b) and 103(a). However, several points raised in said arguments and Declaration will be addressed below.

The arguments of applicants and Declarant concerning the teachings of the Ogawa et al. reference appear to revolve around the pore sizes in the ultrafiltration membranes. Applicants and Declarant indicate that Ogawa et al. uses in their working example a filter with a pore size of 0.035 microns while applicants and Declarant indicate that their use of filters with larger pore sizes unexpectedly retains nucleic acid molecules that would ordinarily be expected to pass through the filters. Applicants and Declarant also assert that since the method of Ogawa et al. produced highly purified phage DNA, there would be no reason to modify said method with the instant procedures using membranes with pore sizes that are larger than those employed in ultrafiltration of biomolecules.

In response the examiner notes that applicants and Declarant appear to be basing their arguments on limitations concerning the pore sizes of the membranes which are not recited in the pending claims. The only claimed limitations concerning the pore sizes (in claims 82 and 90-91) recite membranes which can have pore sizes in the range of 0.001 to 50 or 0.01 to 20 or 0.05 to 10 micrometers. Applicants' and Declarant's arguments on this issue are therefore not persuasive.

Applicants and Declarant appear to argue the teachings of the secondary references in isolation. Applicants and Declarant's arguments concerning the membranes used in the Pfister et al. reference (in the RNeasy® products) are not germane to the purpose for which the Pfister et al. reference was applied, i.e. to demonstrate the use of standard solutions in lysing cells and immobilizing nucleic acids on filters. Likewise, applicants and Declarant's arguments with regard to the Boom et

al. reference do not address the rationale by which the examiner combined the references. It is noted that with regard to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Miscellaneous

Claims 65-66 have not been considered in this Office Action as the status identifiers for these claims are improper (i.e. "not entered"). It is unclear whether applicants seek to have these claims considered or whether the claims are meant to be canceled. These claims will stand as objected to. Clarification on this issue is required.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
July 30, 2007

DAVID GUZO
PRIMARY EXAMINER